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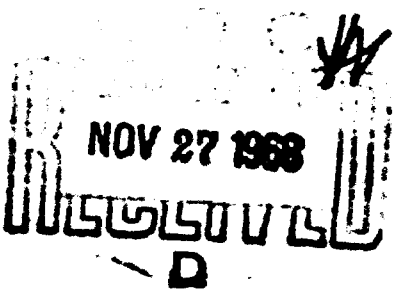

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ESTABLISHING PERMISSIBLE MAXIMUMS IN THE CONTENT AND INGESTION LEVELS OF RADIOACTIVE ISOTOPES IN THE ORGANISM

-USSR-

[Following is the translation of an article by Yu. I. Moskalev in the Russian-language periodical Meditsinskaya Radiologiya (Medical Radiology), Vol 7, No 8, Moscow, August 1962, pages 91-97.]

In order to establish permissible levels for the ingestion of radioactive isotopes in the organism, an understanding of general laws of biological activity for small ionizing radiation doses is necessary. Among the basic foci of radiobiology, an important place is occupied by problems of threshold, summation, restoration, compensation, and radiosensitivity in their various aspects. An understanding of laws governing distribution, accumulation, and removal of radioactive isotopes from the organism in relation to the rhythm of their ingestion — is another, but no less important, aspect of this question.

In this article we wish to examine possibilities of experimental bases for permissible maximums in the content and ingestion levels of radioactive isotopes in the human organism, while using osteosarcomagenic and leukemogenic action of radioactive isotopes as the criterion for longevity.

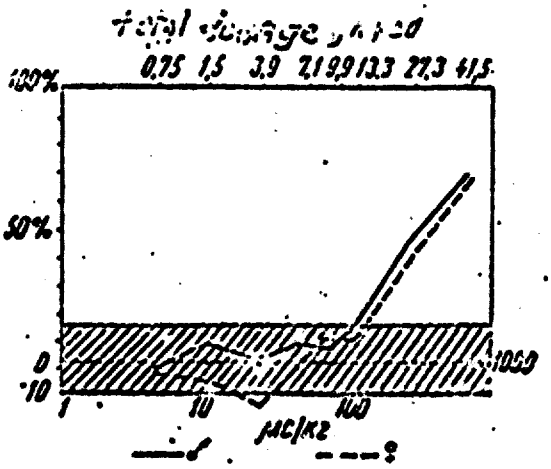
The high energy level of irradiation, significantly exceeding that of chemical ties, makes the hypothesis highly likely that there is no threshold for the action of ionizing radiation in initial changes in any structure of the organism on a molecular level. It does not follow, however, that reactions at other levels also have no threshold. Experimental evidence on the biological activity of various aspects of ionizing radiation, including radioactive isotopes, is sufficiently convincing on this score.

In resolving the problem of the threshold or non-threshold nature of the reaction, data concerning the form of the dose-effect curve are highly significant.

Figure 1 presents data characterizing the degree of decrease in the natural life span of rats in relation to the amount of Sr^{90} induced into the abdominal cavity. We see that, according to the criterion of

life span duration, the action of Sr^{90} has a threshold character. Analogous results were obtained with other radioactive isotopes, as for instance Co^{144}, Cs^{137}, Ba^{140} and others. There exists a very wide dosage diapason which does not affect the longevity of experimental rats. The maximal Sr^{90} dosage that is ineffective for rats, according to the criterion of longevity, is 25-50 μc/kg; and for mice (according to the data of M. Finkel') — 4 μc/kg.

Figure 1. The average decrease in the life span of rats (in percentages to control) in relation to the quantity of intra-abdominal induction of Sr^{90}.



Legend: The striped area — death rate for control animals with reliability intervals for P = 0.05.

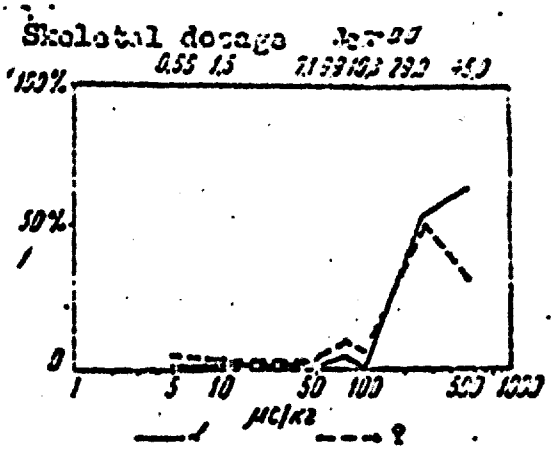
We are acquiring experimental data providing evidence that, at small quantities of radioactive substances, the average life span of experimental animals increases. For instance, on induction of Sr^{90} in quantities of 1-5 per rat, the experimental animals initially die off more slowly than the control animals. In 500 days, 36.6% of the control animals died, while on induction of 1, 2, and 5 μc the corresponding percentages were 25.8, 30.9, and 17.2%. The average life span of female rats in experimental groups was 530, 536, and 585 days; while in the control — 506 days. Analogous results were obtained with Ce^{144}. In parenteral induction of this isotope in quantities of 1, 2, 5, and 10 , by the 450th day there died 7.9, 7.7, 13.2, and 8.8% of male rats and 14.3, 12.2, 17.9, and 17.1% of female rats. In the control group, for the same time interval 21.4% male rats and 28.6% female rats died. The differences between the death rates for control and experimental groups are reliable. Radiation levels for the animals at the quantities of Ce^{144} were comparatively low. The average daily dosage strength on induction

of 1-5 μc Ce^{144} was 0.8-3.4 rad/day, and in bone tissue 1.3-5.2 rad/day. The average irradiation dose, accumulated during the life span, was 0.03-0.16 krad, and in bone tissue -- 0.04-0.6 krad. M. Finkel's research also emphasizes the long, in comparison with adequate control, life span of mice subjected to small quantities of Pa^{239}, U^{232}, and Po^{210}.

We are dwelling in some detail on this data as we are deeply convinced that in evaluating permissible levels of content and ingestion of radioactive isotopes in the organism it is appropriate to use not just any reaction of the organism to irradiation, but only those which characterize the injurious action of radiation. Of course, as a result of the fact that under conditions of prolonged action of low radiation levels average life span increase is possible, the causes of death can significantly differ from those in the control population. In this connection we are faced with the difficult problem concerning which deviations from "the norm" in conditions of continuous radiation can be taken into account in the evaluation of harmful effects of small dosage radiation.

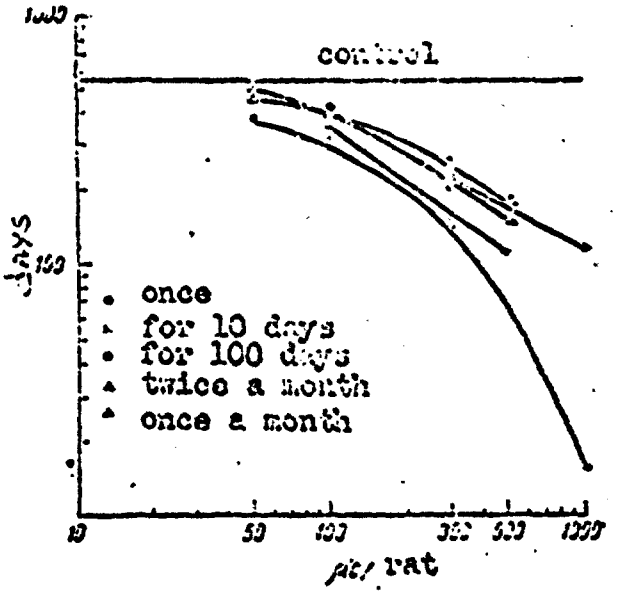
In the evaluation of the injurious action of radioactive isotopes, the data characterizing their blastomogenic activity is very significant. One of the most dangerous of the radioactive isotopes in the professional sense is Sr^{90}. Experiment shows that this radioactive isotope elicits in animals (mice, rats, rabbits, dogs) the appearance of tumors of the bone, and hemopoietic and endocrine systems. Quantitative data, describing the appearance of these tumors in relation to the quantity of induced activity, do not have a linear character. Most frequently Sr^{90} produces bone tissue tumors in animals. This type of tumor reaction has been studied in more detail and can be quantitatively described. Figure 2 shows the "threshold" nature of the indicated effect, in any case for the limited population of experimental animals encompassing hundreds of animals per dose. On single parenterial induction of the isotope, the minimal osteosarcomogenic dose is within limits of 25-50 μc/kg. According to our evidence, on single parenterial induction of rats with Sr^{90}, the ineffective quantity in relation to osteosarcoma is 5-50 μc/kg; according to M. Finkel's mice experiments, it is 4 μc/kg. If we suppose that a similar ratio is true in man, then allowing for differences in life span, single parenterial induction of Sr^{90} in quantitites of 10-100 μc should not affect the natural life span in man nor increase the incidence of bone tissue tumors.

Figure 2. The frequency of osteosarcoma in male and female rats in relation to the quantity of intra-abdominally induced Sr^{90}.



The action of Sr^{90} often produces leukoses. The problem of whether this is a threshold or non-threshold reaction has not yet been resolved. Rats develop leukoses significantly more rarely than sarcomas under the action of Sr^{90}. On inducing Sr^{90} in quantities of 50-250 μc/kg, the frquency of leukoses increases 2-4 times in comparison with the control. The relation of leukoses incidence to the quantity of parenterial rat induction of Sr^{90} is illustrated in Figure 3. The data in this figure indicate the absence of a linear relationship between the quantity of induced Sr^{90} and the frequency of leukoses. The shape of the curve is evidence of the necessity for exceeding threshold dosages in producing leukoses. In Sr^{90} induction in quantities of 5 μc/kg, leukoses are encountered in the same frequency in experimental (in one rat out of 83, surviving 200 days, or 1.2%) and control rats (in 6 out of 337, or 1.8%). These rats sustain an irradiation dose of 0.27 krad in their bone marrow during their lifetime.

Figure 3. The average life span of rats in relation to the ingestion rhythm and Sr^{90} dosage.



According to the influence of radioactive isotopes on the life span and the appearance of tumors in the hemopoietic tissue and bone, the action of Sr^{90} and other osteotropic isotopes has a threshold character. This provides a basis for future consideration of the problem of permissible levels of content and ingestion for radioactive isotopes in the organism for a few people at least, whose work is related to the utilization of radioactive isotopes.

Because of the slow removal from the organism of the injurious action of radioactive isotopes, even their single ingestion into the organism continues over a very prolonged period; and in the case of long-lived radioactive isotopes -- over a full life span. It is therefore very important to clarify the question of the role of the time factor in the injurious action of radioactive isotopes, and the relationship of their biological activity to the ingestion rhythm of the organism.

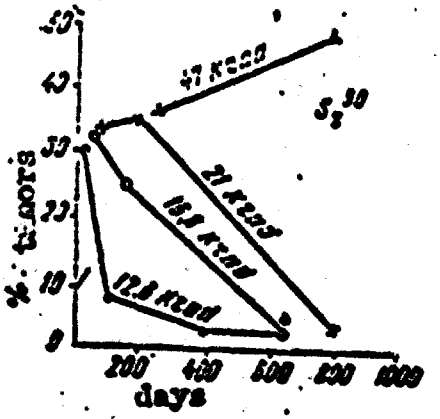
A very complex correlation exists between the organism's reactions and ionizing radiation's action rhythm. At the basis of the correlation lies the differing sensitivity of separate systems and organs to irradiation, and their varied capacity for compensation, restoration, and summation of irradiation injury. Restorative processes occur differently in various systems of the organism, so that a decrease of dosage strength can have unequal significance for various systems. Ovaries have a very high sensitivity to ionizing irradiation and a very low reparative capacity. In contrast to hemopoietic organs and the intestinal mucous membrane, the ovaries show destructive changes of a single type on single massive, and prolonged, action.

A comparative evaluation of the action of $Sr^{89,90}$ on the life span of rats in relation to the isotope ingestion rhythm indicates incomplete summation of radioactive effects. Protracted induction (daily for 100 days at 15 μc) of highly effective single doses (1,500 μc per rat, intraabdominally) of $Sr^{89,90}$ leads to a significant decrease (by 10 times) in comparison with the control (473 ± 21 days) of the life span (from 19 ± 4 at a single induction to 160 ± 20 days at prolonged ingestion). It is important to emphasize that such an abrupt decrease in the effective action of radioactive isotopes on protracted ingestion into the organism is observed only under the breakdown of highly effective quantities. On breakdown of acute and chronic effective isotope quantities, differences in the life span in relation to isotope ingestion rhythm are less marked (See figure 3). In later intervals of the experiment there are similar peripheral blood changes in the animals, irregardless of single or prolonged induction of the indicated quantity of Sr^{90}.

It is of interest to evaluate the significance of dosage strength in the occurence of histogenic action from ionizing radiation. An analysis of experimental data shows that, under the action of Sr^{90}, the incidence of osteosarcom significantly depends on dosage strength (Figure 4) [See Note] . Within limits of equal total doses (12.6-21 krad), decreasing dosage strength by 20 times produces a decrease of osteosarcoma incidence by 10 times. When the bone marrow accumulates 12.6 krad for 30, 100, and 400 days, osteosarcomas occur in 30; 8, 4, and 2.6% of the animals. Within limits of optimal osteosarcomogenic doses (47 krad), decreasing the irradiational dosage strength by 3 times has little reflection on the total incidence of osteosarcomas.

([Note]: Text of footnote: The frequency of osteosarcomas under the given total irradiation dosage was not determined immediately after the bone marrow accumulated a corresponding dose, but after the "latent" period elapsed (200 days) necessary for development of the tumor. Thus, for example, at total doses of 16.8 krad accumulated by the skeleton over 50 days, the osteosarcoma frequency induced by this dosage was determined on the 250th day, i.e. after completion of the "latent" period.)

Figure 4. The relation of the incidence of sarcomas in rats under the action of Sr^{90} to the strength and magnitude of the total irradiation dose in bone tissue.



Corresponding to these data are the experiments on the study of the relationship between osteosarcomogenic Sr^{90} action (Kuzma and Zander, 1958) and $S.^{90}$ (Yu. I. Moskalev) in relation to the isotope ingestion rhythm of the organism. In our experiment, conducted with V. N. Stral'tsova, it was established that in single Sr^{90} induction (in equilibrium with Y^{90}) at quantities of 100 μc per rat, osteosarcomas develop in 26%; on induction of the indicated quantity for 100 days — in 8.3%; and on fractional induction at 2 week intervals (for 10 inductions) and one month (5 inductions), the rats did not develop osteosarcomas. We must state that the "latent" period necessary for the development of osteosarcomas increases with a decreased quantity of induced activity.

These facts are evidence that, under low radiation levels in structures where deleterious changes are occurring, restorative processes take place. This means that radiation summation is incomplete. Under the action of α-radiation, bone tissue restorative processes occur much more weakly than under β-irradiation. For example, according to the observations of M. Finkel' (1956), under the action of Ra^{226} a decrease to 1/10th (from 60 to 5 μc/kg) of the amount of induced isotope (in experiments with mice) leads to a decrease in incidence of osteosarcoma from 60 to 35%, i.e. it lessens to half. In the case of Pu^{239}, on decrease of the optimal osteosarcomogenic dose from 3 to 0.3 μc/kg, the frequency of osteosarcoma decreased to 1% . Research on Pu^{239}, conducted on rats by A. M. Bukhtoyarova and V. K. Lemberg, shows that under a decreased quantity of induced activity to 1/10th (from 6.3 to 0.63 μc/kg) the frequency of osteosarcoma decreases to 40%. There is an utterly different correlation under the action of β-irradiation (Yu. I. Moskalev). A decrease to 1/10th of optimal osteosarcomogenic quantities of Sr^{90} and Ce^{144} (from 50-1,000 to 50-100 μc/kg) is associated with a drop in frequency of osteosarcoma to 3.3-2%, or to an order higher than under α-irradiation.

Table 1. Bone tumor frequency under parenteral induction of Pu^{239} under various isotope ingestion rhythms (according to the data of Yu. I. Moskalev, L. A. Buldakov, and V. N. Stral'tsova)

1. Изотоп 2.	Количество, μc/кг 3.	4. Ритм введения: однократно 4.	за 50 дней 5.	за 100 дней 6.	один раз в неделю по 9 недель 7.	один раз в 2 недели за 18 недель 8.
Pu^{239}	1,25—20	2/46 (4,4%)	4/43 (9,3%)	3/45 (6,7%)	5/36 (13,9%)	3/20 (15%)
$Sr^{90}+Y^{90}$	500	6/23 (26%)		1/12 (8,3%)	0/14 (0)	0/11 (0)

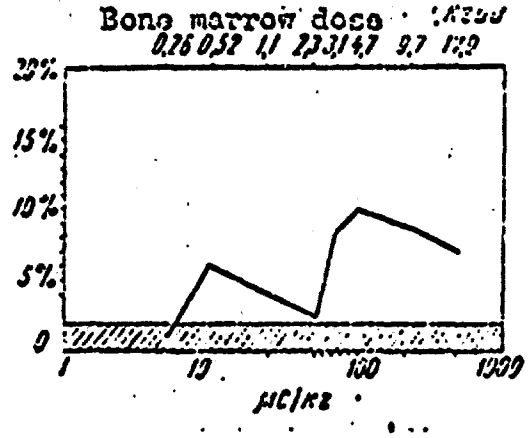
Legend: 1. Induction rhythm. 2. Isotope. 3. Quantity μc/kg. 4. single 5. for 50 days 6. for 100 days 7. once weekly for 9 weeks 8. once in 2 weeks for 18 weeks.

Note: the numerator — tumor frequency; the denominator — the quantity of animals not surviving after the 200th day.

In contrast to Sr^{90}, the osteosarcomagenic action of Pu^{239} is not too dependent on the ingestion rhythm of the isotope into the organism. It was shown that under Pu^{239} action bone tumors occur both with single and prolonged ingestion of equal isotope amounts (Table 1).

One forms the impression that, under prolonged induction of Pu^{239}, bone tissue tumors develop even somewhat more frequently than under single induction. For example, after single induction of Pu^{239} in quantities of 1.25 to 20 μc, bone tumors developed in 4.8% of the rats who did not survive after the 200th day; on induction of the same quantities for 50 and 100 days, 9 weeks (once weekly) and 18 weeks (once every two weeks), bone tumors developed correspondingly in 8.9, 6.7, 13.9, and 15%. Since our data are quantitatively small, further experiments according to this plan are necessary on a larger sample of animals. Nevertheless, results of our research permit our making the conclusion that the frequency of bone tumors on fractioned and protracted induction of α-irradiators does not, in any case, decrease. These data are evidence that injury produced by α-irradiators are less well restored and better summated under protracted action. The indicated differences in blastomogenic activity of α- and β-irradiators is a necessary factor to consider in attempts to extrapolate from experimental results on animals to humans.

Figure 5. The relation of leukoses frequency to the quantity of induced Sr^{90}.



Legend: Striped area -- leukoses frequency in control rats.

In contrast to osteosarcomas, the frequency of hemopoietic tissue tumors under Sr^{90} in conditions of protracted action does not decrease. On the contrary, it can even be greater than in concentrated action. For example, at total doses of 2.7 krad accumulated by bone marrow over 50 days, leukoses under Sr^{90} developed in 1% of the rats; under accumulation of the indicated dose for 200 and 600 days — in a corresponding 3.3 and 5.6% of animals. At total dose of 5.6 krad, leukoses frequency at accumulated doses for 50, 150, and 650 days was 2.5, 4.5 and 8.3 % (Figure 5).

These facts point to the existence of summation and poor restoration of injuries in bone marrow cambial elements leading to the occurrence of leukoses.

The data we have examined led us to the conclusion that under prolonged ingestion of small quantities of Sr^{90}, the probability of the occurrence of osteosarcoma decreases. The existence of a definite "threshold" dose, necessary for the induction of sarcomas, and the abrupt decrease in the frequency of bone tumors under decreased dosage strengths, provide a basis for the position stated above. The existence of more complex conditions for the occurrence of leukoses, the existence of a "threshold" dose, and the poor restoration of injuries in bone marrow cells as a consequence of the significantly longer human life span do not exclude the possibility of the occurrence of this reaction under smaller Sr^{90} quantities than those for rats. It is obvious that future accumulation of experimental data is necessary to pin-point minimal leukemogenic doses and the role of the time factor in the production of this reaction.

Leukemogenic radioactive isotope action cannot be examined apart from other reactions of the organism. If we use, as such an additional criterion, the average life span of rats dying from leukosis in the control and experimental groups, then induction of minimal leukemogenic quantities of Sr^{90} (2 μc per rat) produces leukoses in 5 out of 82 rats (6.1%). The average life span of rats with leukoses was 591 days and was even somewhat longer than in control animals (538 days).

Taking Sr^{90} as an example, we will examine ways of translating experimental data from animals to humans. The experimental data indicated above concerning the effect of Sr^{90} on the life span and on the occurrence of tumors of the bone and hemopoietic system can be utilized for the evaluation of minimal permissible levels of the ingestion of this isotope by the human organism. They show that single parenteral Sr^{90} induction in 10 μc quantity does not affect the natural life span or the frequency of bone tumors and leukoses in the human. In recomputing experimental data from animals to humans, owing to the significant differences in longevity, the quantity of Sr^{90} that is non-effective for rats decreases to 2.85%. This means that the same decrease holds for the irradiation dose strength in the rat's organ. For reactions (longevity, bone tumors) which are well restored and weakly summated under protracted action, this has great importance as the additional biological coefficient of reserve plays a part here. For those reactions whose development is little affected by decrease of dosage strength (leukoses, ovarian injuries), this circumstance apparently will have less meaning.

The bone tissue has a prolonged retention not of all the strontium, but only of a portion of it. An analysis of data on distribution shows that rat bone at final stages of the experiment retains 15-20% of the induced Sr^{90}. The maximal permissible Sr^{90} content in human bones, therefore, should be 1.5-2 μc. A similar magnitude (2.3 μc) was obtained in computing the maximal permissible Sr^{90} content in the human body by empirical equation.

(1) $Mpc = 4.6\ d$

where Dpc is the maximal permissible content of osteotropic isotope in the human skeleton; d is the optimal osteosarcomogenic irradiation dose for rats (in microcurie per 1 g).

Equation (1) is derived from the comparison of clinical and experimental investigations on osteosarcomogenic action of radium.

Table 2.

Isotop	2. Оптимальное количество, при котором происходит индукция остеосаркомы, μc/г	3. Предельно допустимое содержание изотопа в скелете человека, μc/г
Sr^{89}	0,5	2,3
Sr^{90}	1,0	4,6
Ba^{140}	1,6	7,3
Y^{91}	1,0	4,6
Y^{90}	3,0	14
Ce^{144}	0,5	2,3
Pm^{147}	3,4	15,8
La^{140}	10,3	45
Pu^{239}	0,005	0,023

Legend: 1. isotope
2. optimal osteosarcomogenic content on intraperitoneal induction, μc/g
3. maximal permissible isotope content in the human skeleton, μc/g.

Table 2 presents magnitudes of maximal permissible contents derived from equation (1) for a number of reactive isotopes in the human body.

The magnitudes of maximal permissible radioactive isotope content thus found are in correspondence with international recommendations.

In evaluating the maximal permissible Sr^{90} content in the human skeleton derived through other methods, including dosimetry, taking into account the unequal distribution of the isotope in the bone tissue and the differences in the magnitudes of local tissue dosages connected with this, we obtain similar magnitudes (1.8-3.7 μc). On conducting corresponding computations for the maximal permissible strength, we used a dosage equal to 300 mber/week.

Once the magnitude of maximal permissible radioactive isotope content has been established in the critical organ, we can go on to an examination of the problem of the activity amounts that can be ingested daily by the organism with food products or through respiratory channels. Until the present time, information on the continuous deposit and removal of radioactive isotopes from critical organs has been gleaned primarily from investigations of single inductions of a substance. Recent research, however, indicates that this method of evaluating maximal permissible levels of radioactive isotope ingestion by the organism is not effective.

We will illustrate this through taking Sr^{90} as an example. In ex-

periments with intra-peritoneal induction of rats, it was found that after single induction, its removal from bone tissue can be satisfactorily described by the equation:

$$(2)\quad Q_t = 25.5\, e^{-0.017t} + 36.6\, e^{-0.0018t}$$

Moreover 41% of the initial Sr^{90} deposit is removed with $T_{biol.} = 40$ days and 59% — with $T_{biol.} = 392$ days.

In conditions of prolonged ingestion (daily induction for 100 days). there are changes not only in the constant removal of the isotope from bones, but, what is particularly important, there are changes in the coefficients of Sr^{90} storage in the bone tissue. Equation (3) describes changes in Sr^{90} content in rat skeleton after isotope induction is stopped:

$$(3)\quad Q_t = 8.6\, e^{-0.009t} + 18.5\, e^{-0.00015t}$$

Nearly 32% of Sr^{90} is removed with $T_{biol.} = 77$ days, and 68% — with $T_{biol.} = 14,600$ days (the magnitude is apparently over-estimated; the observation period after cessation of induction was only 340 days). In comparison with single induction at prolonged ingestion, the magnitude of Sr^{90} storage in the skeleton was 43.5% lower. On fractional induction of Sr^{90} (once a month for a total of 5 inductions), its removal from the skeleton (after cessation of induction) is described by the equation:

$$(4)\quad Q_t = 13.9\, e^{-0.0264t} + 17.1\, e^{-0.00041t}$$

Nearly 46% of the activity is removed with $T_{biol.} = 26$ days and 54% — with $T_{biol.} = 1,690$ days. In comparison with single induction, Sr^{90} content was 50% less.

The indicated data is sufficiently clear evidence that the constant bone deposition and removal of Sr^{90} depends on the rhythm and ingestion of isotope induction into the organism. Moreover the magnitude of Sr^{90} deposition in bone tissue, in conditions of prolonged ingestion, significantly decreases. As a result of the constant deposition and removal of Sr^{90} from the skeleton depending on the rhythm of its induction into the organism and changes in time, it would be inadvisable to draw conclusions regarding laws of isotope deposition in the organism on the basis of experimentation with single induction. There is an obvious necessity for direct data on the patterns of radioactive isotope deposition under prolonged ingestion into the organism.

Under prolonged ingestion of radioactive substances, as a result of radioactive breakdown and removal, an equilibrium is established between isotope ingestion and retention in the organism. Apparently deposition multiplicity (the relation of isotope retention in the organism in a critical organ after an equilibrium has been established to the daily ingested dose) and the speed with which various isotopes achieve an equilibrium will differ. In the case of isotopes having a short period of partial breakdown (for example, Sr^{89} with $T_{\frac{1}{2}} = 53$ days), but a long period of removal from the organism, the problem is resolved re-

latively simply, as their deposition multiplicity in the organism is determined by the partial breakdown period, and the equilibrium between ingestion and deposition of the isotope in the organism is established relatively quickly. The research of E. B. Kurlyandskiy and co-authors (1957) and D. I. Ilyin and Yu. I. Moskalev (1959) conducted on various animals confirm this position. It appeared that Sr^{89} deposition multiplicity in the bone tissue of rats and rabbits is 8.4, and the equilibrium between isotope ingestion and retention in bones was established by the 130th day. Subsequent daily Sr^{89} induction over 830 days did not affect the magnitude of deposition multiplicity of this isotope in the skeleton. On the basis of these data, it is not difficult to calculate that for retention in human bones of maximal permissible Sr^{89} content (2 μc), there can be daily ingestion of 0.2 μc of this isotope. In the case of long-lived radioactive isotopes which are slowly removed from the organism, including Sr^{90}, the equilibrium between ingestion and deposition is established at later intervals.

By means of calculations, we found, along with D. I. Ilyin, that in pigs and dogs, on daily Sr^{90} ingestion, per os equilibrium (99%) must be established in approximately 1,300 days, while the isotope deposition multiplicity is equal to 45. A similar magnitude for Sr^{90} deposition multiplicity in the skeleton, 15, was obtained in experiments on dogs by L. N. Burykina, inducing animals with Sr^{90} by mouth over a period of several years. In conditions of continuous ingestion through the gastrointestinal tract, the Sr^{90} deposition multiplicity in the human skeleton would apparently differ little from the magnitudes indicated above, particularly in the case where Sr^{90} would be ingested by an adult human.

The indirect data confirms the accuracy of the indicated position. We will therefore utilize data on the deposition of stable strontium in the human organism. We know that man consumes 10^{-3} g of stable strontium with his food per day, while the whole human organism retains 0.14 g of this isotope. It therefore follows that under prolonged ingestion, the strontium content in the whole skeleton will exceed the daily ingested quantity by 140 times. A similar magnitude of Sr^{90} deposition multiplicity in the human skeleton is obtained in the comparison of the exchange characteristics of the indicated element with stable calcium. We know that the passage of Sr^{90} from food into bone is achieved with its discrimination in relation to calcium. On the basis of the research of L. A. Buldakovskiy and Yu. I. Moskalev (1960) conducted on sheep, as well as direct observation of the migration of Sr^{90} falling on the earth's surface along the food chain (milk -- bones of new-born children), this coefficient is determined to be 0.2-0.25. These data are evidence that, in comparison with calcium, Sr^{90} is ingested and retained by the organism in smaller amounts.

Sr^{90} deposition multiplicity in the human skeleton will apparently be smaller by the magnitude of its discrimination in relation to calcium. Since calcium deposition multiplicity is 1,000, the corresponding magnitude for Sr^{90} should be 200-250. Such Sr^{90} deposition multiplicities might be observed if the isotope had been ingested by the organism from childhood. When Sr^{90} is ingested by the adult human, its deposition

multiplicity should be lower than these magnitudes and similar to that obtained in experiment. If we take as a base a maximal Sr^{90} deposition multiplicity of the human skeleton of 250, then for the skeleton to retain the maximal permissible magnitude (2 μc) of this isotope there must be a daily induction of 0.008 μc. This magnitude is 4.4 times higher than the one recommended by the International Commission on radiological protection (0.0018 μc).

On this basis we can conclude that existing norms of maximal permissible content and ingestion of Sr^{90} in the human organism have experimental verification and indicate the existence of a sufficient reserve guarantee.

The induction of maximal permissible Sr^{90} quantities into the organism cannot present great dangers in the genetic sense. In any case, this danger is significantly less than that from the naturally radioactive isotopes K^{40} and C^{14} which constantly enter the organism with food intake. For example, the adult human daily takes in 0.0054 μc of naturally radioactive isotope K^{40} and C^{14}, which is 3.2 times greater than the maximal permissible magnitude of Sr^{90} ingestion (0.0018 μc). In comparison of the indicated magnitudes, we must keep in mind that K^{40} and C^{14} are wholly ingested from the gastro-intestinal tract and are comparatively evenly distributed in organs and tissues, while Sr^{90} is only partially ingested from the gasto-intestinal tract and is selectively retained by bones, when soft tissues retain only an insignificant portion.

The data cited indicate that further research is necessary, directed at studying the radiobiological laws of the action of ionizing radiation in small doses; establishing permissible retention levels (in the critical organ) of radioactive isotopes and their ingestion by the human organism; and studying the laws of their deposition and removal under prolonged ingestion by the organism.

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